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Prognostic value of ALBI score in lung cancer patients with liver metastases and hepatic failure: a single-center experience

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ABSTRACT

Aims: Lung cancer remains the leading cause of cancer-related mortality worldwide, with especially poor outcomes in the metastatic stage. Liver metastases and subsequent liver failure significantly worsen prognosis. Accurate risk stratification is therefore essential in this setting. The albumin-bilirubin (ALBI) score, a simple and objective indicator of liver function, may aid in prognostic evaluation. Unlike previous studies, this study specifically focuses on lung cancer patients with liver failure, a clinically distinct and high-risk subgroup.

Methods: Clinicopathological data and laboratory parameters were retrospectively retrieved from the hospital information system for patients with histologically confirmed lung cancer and concurrent liver metastases complicated by liver failure. ALBI score was calculated based on peripheral blood test results using the formula: (0.66×log10[bilirubin, μmol/L])−(0.085×albumin, g/L).

Results: The median overall survival (mOS) was 0.19 months in ALBI grade 3 (95% CI: 0.10–0.28) and 1.54 months in ALBI grade 2 (95% CI: 0.19–2.89), with a statistically significant difference ($p<0.01$). Univariate analysis identified NSCLC histology, ALBI grade 3, and chemotherapy during hepatic failure as significant predictors of overall survival. In multivariate analysis, chemotherapy (HR: 0.11, $p<0.001$) and ALBI grade 3 (HR: 2.31, $p=0.008$) remained independent prognostic factors.

Conclusion: ALBI score is a useful prognostic marker for survival after liver failure, with ALBI grade 3 indicating worse outcomes. It may aid in risk stratification and clinical decision-making in this high-risk group.

Keywords: ALBI, albumin, bilirubin, lung cancer

INTRODUCTION

Lung cancer is one of the most commonly diagnosed malignancies worldwide and remains the leading cause of cancer-related mortality in both sexes.[1] Small-cell (SCLC) or non-small-cell (NSCLC) lung cancer , frequently metastasizes to various organs in advanced stages, including the bones, nervous system, respiratory system, and liver. Among these, liver metastases are associated with particularly poor prognosis, chemotherapy and immunotherapy resistance and shorter overall survival (OS). This adverse outcome is thought to be related to both the liver's immunotolerant microenvironment and the relative resistance of hepatic metastases to chemotherapy.[2,3]

In a comprehensive review conducted by Waninger et al.[4] liver metastases were shown to be associated with poor prognosis regardless of the primary solid tumor type. Moreover, this unfavorable clinical outcome was observed not only in patients receiving chemotherapy but also in those undergoing immunotherapy. The same study also highlighted that in patients with NSCLC, the development of liver metastases was linked to worse outcomes, independent of therapeutic interventions. Once liver metastasis develops—particularly in patients progressing to hepatic failure—both treatment options become significantly limited and the prognosis worsens considerably. Moreover, a subset of patients cannot receive any systemic therapy at this stage due to poor performance status (PS) and inadequate hepatic reserve.

Traditional scoring systems such as the Child–Pugh classification and the Model for End-Stage Liver Disease (MELD) score are commonly used to assess liver function. However, their utility in the context of metastatic disease is limited due to the inclusion of subjective parameters and their primary focus on chronic liver diseases. In this regard, the ALBI score, which is based solely on serum albumin and bilirubin levels, has emerged as a more objective, simple, and clinically applicable alternative.[5]

Currently, there is no universally accepted or clinically validated biomarker available in the literature to predict

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prognosis in patients with liver metastases secondary to lung cancer, particularly in those who progress to hepatic failure. In this study, we aimed to evaluate the Albumin-Bilirubin (ALBI) score, which we hypothesize may serve as a valuable tool for both prognostic assessment and guiding treatment decisions in patients with liver metastases complicated by hepatic failure.

METHODS

The study was conducted with the permission of Dr. Abdurrahman Yurtaslan Oncology Health Practice and Research Center Clinical Researches Ethics Committee (Date: 24.08.2022, Decision No: 2022-08/2015). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study was a single-center, retrospective observational study and included liver metastatic lung cancer patients who were admitted to our hospital between 2020 and 2023. The study included patients aged over 18 years who were diagnosed with small cell or non-small cell lung cancer (NSCLC) confirmed by histopathology, and who had liver metastases either at the time of diagnosis or developed them during follow-up.

All patients enrolled in the study exhibited liver failure of varying severity. Liver failure was defined as a total bilirubin level at least 1.5 times the upper limit of normal (ULN), in combination with an elevation in either ALT or AST above the ULN. Patients with liver metastases but without liver failure were excluded from the study.

Patients' age, sex, pathological characteristics, treatments, and laboratory parameters were retrospectively reviewed and recorded using the hospital medical records system.

The ALBI score was calculated using peripheral blood tests according to the following formula: $(0.66\times\log_{10}[\text{bilirubin, }\mu\text{mol/L}])-(0.085\times\text{albumin, g/L})$. Patients were categorized into three worsening grades based on their ALBI scores: grade 1 (≤–2.60), grade 2 (>–2.60 to ≤–1.39), and grade 3 (>–1.39).[6] Due to the inclusion and exclusion criteria of the study, all patients included in the final analysis had elevated bilirubin levels (>1.5×ULN). As a result, none of the patients met the criteria for ALBI grade 1. This distribution reflects the clinical characteristics of the study population.

Statistical Analysis

Survival outcomes were analyzed by using the Kaplan-Meier method, and differences between groups were compared by using the log-rank test. Categorical variables are summarized as frequencies and percentages (n, %), while continuous variables are shown as mean±standard deviation or median (range), depending on the distribution. Variables found to be statistically significant (p≤0.05) in univariate analyses were included in the multivariate regression model to determine the independent determinants of the outcome. A p-value of <0.05 was accepted as the threshold for statistical significance. We used SPSS version 25.0 (IBM Corp., Armonk, NY, USA) to perform all statistical analyses.

RESULTS

Fifty-eight patients were included in the study. The median age was 70 years (min-max:49–77). The demographic characteristics of the patients are presented in **Table 1**. 75.9% (n=44) of the patients were male and 24.1% (n=14) were female. Among patients who developed liver failure, 36.2% (n=21) were able to receive systemic treatment after the onset of liver failure. Of patients 60.3% (n=35) had small cell lung cancer, while 39.7% (n=23) had NSCLC. Patients with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) between 1 and 4 were included in the study. The majority had an ECOG PS of 3 (56.9%, n=33), and only two patients had an ECOG PS of 4.

Table 1. Demographic characteristics of the patients

Clinical and demographical features of patients (after hepatic failure)		**Total n:58 (%)**
Gender	Male	44 (75.9)
	Female	14 (24.1)
Age	<65	34 (58.6)
	≥65	24 (41.4)
ECOG (at the time of hepatic failure diagnosis)	1	11 (19.0)
	2	12 (20.7)
	3	33 (56.9)
	4	2 (3.4)
Smoking	No	6 (10.3)
	Yes	52 (89.7)
Type of lung cancer	SCLC	35 (60.3)
	NSCLC	23 (39.7)
Number of metastatic sites (at the time of hepatic failure diagnosis)	≤2	17 (29.3)
	>2	41 (70.7)
Chemotherapy (during hepatic failure)	No	37 (63.8)
	Yes	21 (36.2)
ALBI score	Grade 2	26 (44.8)
	Grade 3	32 (55.2)

ECOG: Eastern Cooperative Oncology Group, ALBI: Albumin-bilirubin, SCLC: Small cell lung cancer, NSCLC: Non-small cell lung cancer

According to ALBI score evaluation, 44.8% of patients (n=26) were categorized as grade 2, and 55.2% (n=32) as grade 3 (**Table 1**).

OS analyses were conducted based on the patients' ALBI scores. Following the onset of liver failure, the median OS was 0.19 months (95% CI: 0.10–0.28) for patients with an ALBI grade of 3, compared to 1.54 months (95% CI: 0.19–2.89) for those with an ALBI grade of 2 (p<0.01) (**Figure**).

In the univariate Cox regression analysis for OS after hepatic failure, several variables demonstrated significant associations. Notably, NSCLC (compared to SCLC) was associated with worse survival (HR: 2.24, 95% CI: 1.24–4.03, p<0.01), and patients who received chemotherapy during hepatic failure had markedly improved survival outcomes (HR: 0.10, 95% CI: 0.04–0.25, p<0.01). Additionally, ALBI grade 3 was associated

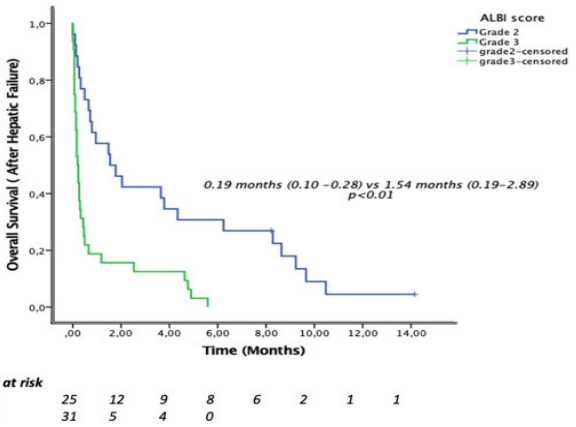

Figure. Kaplan–Meier survival analysis stratified by ALBI grade
ALBI: Albumin-bilirubin

with poorer survival compared to grade 2 (HR: 3.07, 95% CI: 1.69–5.55, p<0.01) (Table 2).

Table 2. Univariate and multivariate Cox regression analyses for overall survival

Overall survival (after hepatic failure)	Univariate Cox regression		Multivariate Cox regression	
	HR (CI 95%)	p value	HR (CI 95%)	p value
Gender Female Male	0.67 (0.35-1.26)	0.21		
Age ≥65 <65	1.13 (0.66-1.93)	0.64		
Type of lung cancer NSCLC SCLC	2.24 (1.24-4.03)	<0.01	0.86 (0.44-1.65)	0.65
Number of metastatic sites >2 ≤2	0.61 (0.33-1.11)	0.10		
Chemotherapy (during hepatic failure) Yes No	0.10 (0.04-0.25)	<0.01	0.11 (0.04-0.28)	<0.01
ALBI Grade 3 Grade 2	3.07(1.69-5.55)	<0.01	2.31 (1.25-4.29)	0.008

CI: Confidence interval, HR: Heart rate, SCLC: Small cell lung cancer, NSCLC: Non-small cell lung cancer, ALBI: Albumin-bilirubin

In the multivariate Cox regression analysis, three variables remained statistically significant. Receiving chemotherapy during hepatic failure was independently associated with improved survival (HR: 0.11, 95% CI: 0.04–0.28, p<0.001). In contrast, an ALBI grade 3 (HR: 2.31, 95% CI: 1.25–4.29, p=0.008) was independently associated with increased risk of mortality (Table 2). Type of lung cancer did not retain statistical significance in the multivariate model. ALBI score and receipt of chemotherapy during liver failure were identified as independent prognostic risk factors.

DISCUSSION

In recent years, ALBI score has been investigated in various solid tumors for its potential to predict prognosis. As is known, albumin and bilirubin are two important biochemical markers in evaluating liver functions. Higher than normal values of bilirubin, a heme breakdown product, indicate liver damage and dysfunction, while albumin reflects and shows the synthesis function, and its low levels are associated with hepatic failure. Therefore, it was thought that this scoring system could be valuable based on these two important parameters.[7,8]

The score initially gained attention in patients with hepatocellular carcinoma (HCC). As is well known, the Child-Pugh scoring system is frequently used to assess prognosis and includes five variables: bilirubin, albumin, INR, ascites, and hepatic encephalopathy. However, the assessment of ascites and encephalopathy involves subjective evaluations. In contrast, the ALBI score is calculated using only two objective laboratory parameters—serum albumin and bilirubin—offering a more standardized and reproducible tool. Due to its objectivity and potential to detect subtle changes in liver function, the ALBI score has garnered increasing interest from researchers.[5]

The potential of the ALBI score to evaluate liver function as effectively as the Child-Pugh scoring system was first proposed by Johnson et al.[9]

After the prognostic value of the ALBI score was first demonstrated in HCC, its significance has also been investigated by several researchers in solid organ tumors across various clinical stages.[10-12] In a study by Zhang L et al.,[12] patients diagnosed with pancreatic cancer and synchronous liver metastases were evaluated. Among those who underwent surgical resection of the primary tumor and received radiofrequency ablation for liver metastases, a low ALBI score was found to be significantly associated with both longer recurrence-free survival and improved OS.

A similar study was conducted by Zhang TN et al.,[13] evaluating the prognostic value of the pretreatment ALBI score in patients with advanced pancreatic cancer. The study suggested that the ALBI score may serve as an independent prognostic predictor. In subgroup analyses, the prognostic significance of ALBI was observed only in patients with liver metastases. Moreover, among patients with a low ALBI score, those who received combination therapy demonstrated better outcomes compared to those treated with monotherapy. Additionally, in colorectal cancer, a high ALBI score has been associated with the development of distant metastases and shorter metastasis-free survival.[14] These findings suggest that the ALBI score may be a useful tool in guiding prognosis and treatment decisions. Unlike previous studies, a key strength of our work is the limiting the study population to those with hepatic failure. While prior studies also enrolled individuals with preserved liver function, they similarly identified elevated ALBI scores as indicators of poor prognosis, consistent with our results.

The administration of chemotherapy in the setting of visceral crisis and hepatic failure is not a commonly adopted approach in medical oncology. Clinical guidelines often recommend discontinuation of treatment and follow-up without active therapy at this stage. In the article by Koren et al.,[15] it was emphasized that elevated bilirubin and hepatic enzymes may alter the pharmacokinetics of certain chemotherapeutic

agents, potentially affecting treatment efficacy. However, to the best of our knowledge, there are no studies in the literature specifically addressing this issue in the context of lung cancer treatment. In our study, receiving chemotherapy during hepatic failure was independently associated with improved survival among patients with lung cancer.

As in other solid tumors, studies investigating the ALBI score in lung cancer are also available in the literature. In a study involving NSCLC patients who underwent surgery for stage IA–IIIA disease, patients were stratified into ALBI grade 1 and grade 2/3 groups. The results demonstrated that various clinicopathological features—such as older age, smoking history, histological subtype, advanced pT stage, and higher disease stage—were significantly associated with higher ALBI scores. Moreover, patients with ALBI grade 2/3 had significantly worse disease-free survival (DFS), OS, and cancer-specific survival (CSS) compared to those with ALBI grade 1. Over a five-year follow-up period, the DFS rates were 65.6% vs. 80.3% ($p<0.0001$), OS rates were 77.6% vs. 91.0% ($p<0.0001$), and CSS rates were 85.3% vs. 93.3% ($p=0.0005$), respectively.[16]

In another study involving patients with advanced-stage NSCLC receiving immunotherapy, in addition to PD-L1 expression, treatment modality (monotherapy versus combination therapy), NLR and PD-L1 levels, ALBI score was identified as an independent prognostic factor for both progression-free survival (PFS) and OS in multivariate analysis. In this analysis, the hazard ratios for ALBI grade 2 versus grade 1 and grade 3 versus grade 1 were 1.60 and 5.22, respectively, with statistical significance ($p<0.0001$).[17] Similar findings regarding the impact of ALBI score on survival were also observed in the study by Matsukane et al.,[18] which included patients with advanced-stage NSCLC receiving immunotherapy. Similarly, another study on NSCLC patients undergoing immunotherapy assessed the prognostic significance of PS and the ALBI score, reporting consistent findings. It was emphasized that the combination of ALBI score and PS may serve as a strong prognostic indicator.[19] In our study, findings consistent with previous literature on ALBI score in lung cancer were also observed when the analysis was limited exclusively to patients with hepatic failure. The association between elevated ALBI scores and poor survival was further supported by a 2024 meta-analysis by Jiang et al.,[6] which included data from 2.057 patients with both SCLC and NSCLC.

Building on the promising findings of previous research, we designed a study specifically focusing on lung cancer patients with liver metastases who subsequently developed hepatic failure—a population not isolated in prior studies. This distinction sets our work apart from existing literature, which predominantly includes patients with preserved liver function. Our study included only patients with ALBI grade 2 and grade 3. Consistent with previous literature, a higher ALBI score was associated with shorter OS.

Limitations

This study has several limitations. First, its retrospective and single-center design may limit the generalizability of the findings. Second, due to the specific focus on patients with hepatic failure, the sample size was relatively small, which may reduce the statistical power of subgroup analyses. Considering the limited sample size subgroup analyses comparing treated versus untreated groups (e.g., different treatment modalities) could not be performed. However, such analyses would be valuable and are recommended for future studies to further strengthen the evidence and contribute to the literature. Third, potential confounding factors such as prior liver-directed therapies, variations in systemic treatment regimens, and unmeasured comorbidities could not be fully controlled. Additionally, the proportion of patients with ECOG PS 3–4 was notably high in our study population. This may affect the generalizability of our findings and should be acknowledged as a limitation of the study.

CONCLUSION

The patient cohort in our study primarily consisted of individuals with poor PS, multiple metastatic sites, and liver failure secondary to hepatic metastases. We hypothesized that the ALBI score could serve as a valuable prognostic tool in guiding the management of this clinically fragile population, and our findings support this assumption. Furthermore, the receipt of chemotherapy during liver failure also emerged as an independent prognostic factor. These results collectively suggest that, even in the setting of hepatic failure, the ALBI score may aid in identifying selected patients who could benefit from systemic treatment over best supportive care. This hypothesis merits further investigation in future studies.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of Dr. Abdurrahman Yurtaslan Oncology Health Practice and Research Center Clinical Researches Ethics Committee (Date: 24.08.2022, Decision No: 2022-08/2015).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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